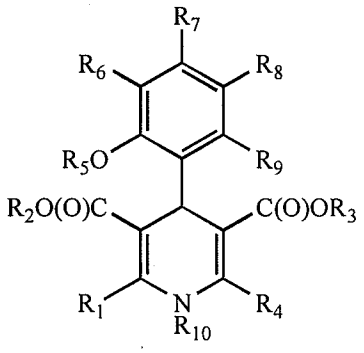
CLAIMS

1. (**Previously presented**) A method for inhibiting calcium T-channel activity, comprising the steps of:

providing a selective T-channel antagonist having an onset of activity in reducing systolic blood pressure *in vivo* of at least three hours and a duration of activity *in vivo* of at least 24 hours, wherein onset of activity refers to the time from administration to maximum reduction of systolic blood pressure, and duration of activity refers to the time from administration until the amount of systolic blood pressure reduction decreases by at least 20 percent; and

administering the antagonist to a mammal in regular doses no more often than once per day, wherein the T-channel antagonist is a compound of Formula I:



(I)

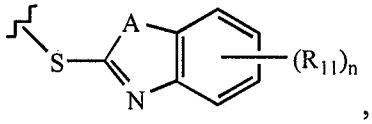
or a pharmaceutically acceptable salt, amide, ester, or prodrug thereof,

wherein

a) R_1-R_8 are each independently selected from the group consisting of hydrogen, halogen, perhaloalkyl, nitro, amino, a diazo salt, optionally substituted lower alkyl, optionally substituted lower alkylene and optionally substituted five-membered or optionally substituted six-membered heteroaryl ring or optionally substituted six-membered aryl or heteroaryl ring,

where the lower alkyl and the lower alkylene moieties are each independently and optionally substituted with one or more substituents

selected from the group consisting of halogen, perhaloalkyl, nitro, amino, hydroxy, alkoxy, sulfhydryl, thioether, cyano, amido, ester, and



,

where A is selected from the group consisting of oxygen, sulfur, and -NH and R_{11} is selected for the group consisting of hydrogen, hydroxy, alkoxy, haloalkoxy, halogen, haloalkyl, perhaloalkyl, nitro, amino, and a diazo salt, and n is between 0-4; and

where the ring moieties are each independently and optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene,

b) R_9 is selected from the group consisting of hydrogen, alkyl, alkylene, and a five-membered or six-membered heteroaryl ring or a six-membered aryl or heteroaryl ring, optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene, halogen, perhaloalkyl, nitro, amino, cyano, amido, and ester;

c) R_{10} is selected from the group consisting of hydrogen and lower alkyl, or R_{10} is optionally not present, in which case the nitrogen-containing ring in the compound of Formula I is pyridine.

2. (**Original**) The method of Claim 1, wherein the T-channel antagonist has a cyclic ring structure with a pendent alkylene group of at least 6 carbon atoms.

3. (**Canceled**)

4. (**Original**) The method of Claim 1, wherein the T-channel antagonist is a prodrug.

5. (**Previously presented**) The method of Claim 1, wherein the T-channel antagonist is selected from the group consisting of:

diethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-carboxypyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto-1'H-benzimidazolyl)methyl-3,5- pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl-3,5- pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl -3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto–1'H-benzimidazolyl)methyl-3,5- pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(2'-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3-ethyl-5-(methoxyethyl)pyridine dicarboxylate;

1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3-methyl-5-(methoxyethyl)pyridine dicarboxylate;

1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2,6-dimethyl-3-isopropyl-5-(methoxyethyl)pyridine dicarboxylate;

1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2,6-dimethyl-3-ethyl-5-(methoxyethyl)pyridine dicarboxylate;

1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2,6-dimethyl-3-ethyl-5-(methoxyethyl)pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4- (2'-methoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-((2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-(2'-aminoethoxy)methyl-6-methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-ethoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-methoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-dinitro-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-ethoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-methoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-isopropoxy-3',5'-diamino-6'-pentadecylphenyl)-2,6-dimethyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-ethoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H- benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

dimethyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diisopropyl 1,4-dihydro-4-(2'-methoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

diethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-(5"-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate;

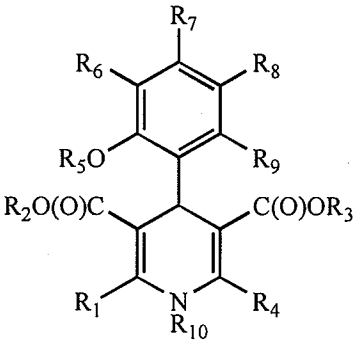
dimethyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-methyl(5'-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate; and

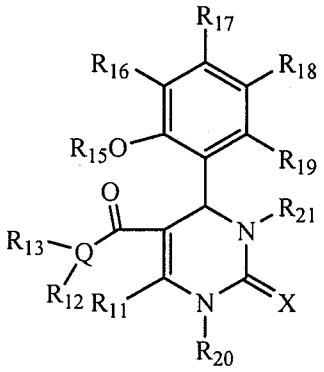
diisopropyl 1,4-dihydro-4-(2'-isopropoxy-6'-pentadecylphenyl)-2-methyl-6-methyl (5'-methyl-2-mercapto-1'H-benzimidazolyl)methyl-3,5-pyridine dicarboxylate.

6. **(Canceled)**

7. **(Withdrawn)** A method for treating hypertension, comprising repeatedly administering to a patient a selective T-channel antagonist in individual dosages spaced at least one day apart.

8. **(Withdrawn)** The method of Claim 7, wherein the T-channel antagonist is a compound of Formula I or II:

(I) 

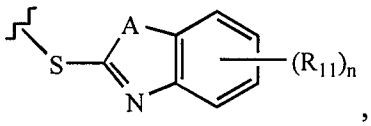
(II) 

or a pharmaceutically acceptable salt, amide, ester, or prodrug thereof,

wherein

a) R_1-R_8 are each independently selected from the group consisting of hydrogen;,halogen, perhaloalkyl, nitro, amino, a diazo salt, optionally substituted lower alkyl, optionally substituted lower alkylene and optionally substituted five-membered or optionally substituted six-membered heteroaryl ring or optionally substituted six-membered aryl or heteroaryl ring,

where the lower alkyl and the lower alkylene moieties are each independently and optionally substituted with one or more substituents selected from the group consisting of halogen, perhaloalkyl, nitro, amino, hydroxy, alkoxy, sulfhydryl, thioether, cyano, amido, ester, and



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where A is selected from the group consisting of oxygen, sulfur, and -NH and R_{11} is selected for the group consisting of hydrogen, hydroxy, alkoxy,

haloalkoxy, halogen, haloalkyl, perhaloalkyl, nitro, amino, and a diazo salt, and n is between 0-4; and

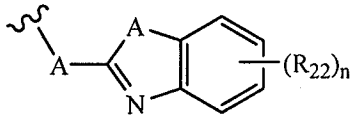
where the ring moieties are each independently and optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene,

b) R_9 is selected from the group consisting of hydrogen, alkyl, alkylene, and a five-membered or six-membered heteroaryl ring or a six-membered aryl or heteroaryl ring, optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene, halogen, perhaloalkyl, nitro, amino, cyano, amido, and ester;

c) R_{10} is selected from the group consisting of hydrogen and lower alkyl, or that R_{10} is optionally not present, in which case the nitrogen-containing ring in the compound of Formula I is pyridine;

d) R_{11}-R_{13} and R_{15}-R_{18}, are each independently selected from the group consisting of hydrogen, halogen, perhaloalkyl, nitro, amino, a diazo salt, optionally substituted lower alkyl, alkoxy, optionally substituted lower alkylene and optionally substituted five-membered or optionally substituted six-membered heteroaryl ring or optionally substituted six-membered aryl or heteroaryl ring, wherein

said lower alkyl and said lower alkylene moieties are each independently and optionally substituted with one or more substituents selected from the group consisting of halogen, perhaloalkyl, nitro, amino, hydroxy, alkoxy, sulfhydryl, thioether, cyano, amido, ester, and



A is selected from the group consisting of oxygen, sulfur, sulfoxide, sulfone, and -NH;

R_{22} is selected from the group consisting of hydrogen, hydroxy, alkoxy, haloalkoxy, halogen, haloalkyl, perhaloalkyl, nitro, amino, and a diazo salt;

n is between 0-4; and

said ring moieties are each independently and optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene,

e) R_{19} is selected from the group consisting of hydrogen, alkyl, alkylene, and a five-membered or six-membered heteroaryl ring or a six-membered aryl or heteroaryl ring, optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene, halogen, perhaloalkyl, nitro, amino, cyano, amido, and ester; and

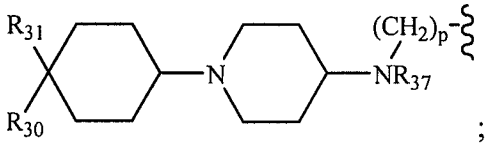
f) R_{20} is selected from the group consisting of hydrogen and lower alkyl

g) R_{21} is selected from the group consisting of:

i) hydrogen, alkyl, alkoxy, alkylene, and a five-membered or six-membered heteroaryl ring or a six-membered aryl or heteroaryl ring, optionally substituted with one or more substituents selected from the group consisting of lower alkyl, lower alkylene, halogen, perhaloalkyl, nitro, amino, cyano, amido, and ester;

ii) COY wherein Y is C_1-C_8 alkyl, C_1-C_8 alkoxy or $NR_{13}R_{14}$, wherein R_{13} is hydrogen or C_1-C_8 alkyl and R_{14} is hydrogen, C_1-C_8 alkyl, or C_1-C_{14} phenalkyl;

iii) X or COX wherein X is



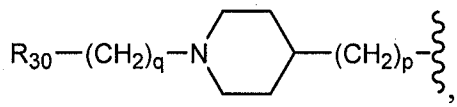
;

iv) halogen, CF_3, cyano, nitro, $COONHR_{35}$, $COON(R_{35})_2$, $COOSO_2R_{38}$, $COONR_{35}SO_2N(R_{35})_2$, CO_2R_{35}, $COON(R_{35})_2$, $COOSO_2N(R_{35})_2$, $COOSO_2R_{38}$.

v) $CONR_{25}R_{26}$, wherein R_{25} is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, or arylalkyl and R_{26} is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, or halosubstituted alkyl, or R_{25} and R_{26} taken together with the nitrogen atom to which they are attached form 1-pyrrolidinyl, 1-piperidinyl, 1-azepinyl, 4-morpholinyl, 4-thiamorpholinyl, 1-piperazinyl, 4-diarylalkyl-1-piperazinyl, each of

which is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkoxy, alkylthio, halo, triflоromethyl, or hydroxy;

vi) Z, COOZ, or C(O)(NH)Z, wherein Z is selected from the group consisting of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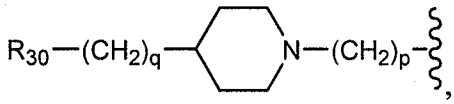
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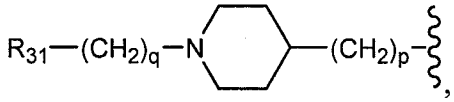
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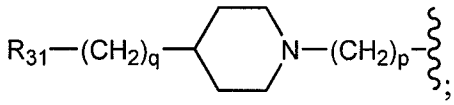
;

wherein

A) p and q are each independently 0-10;

B) R_{30} is phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, CF_3, cyano, nitro, $N(R_{35})_2$, $NR_{35}CONR_{37}$, $NR_{35}CON(R_{37})_2$, $NR_{35}SO_2R_{38}$, $NR_{35}SO_2N(R_{37})_2$, $(CH_2)_{0-4}CO_2R_{35}$, $(CH_2)_{0-4}CON(R_{35})_2$, $(CH_2)_{0-4}SO_2N(R_{35})_2$, $(CH_2)_{0-4}SO_2R_{38}$, and C_{1-4} alkyl;

C) R_{31} is selected from the group consisting of hydrogen, cyano, OR_{38}, $COOR_{35}$, $CON(R_{35})_2$, and phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, CF_3, cyano, nitro, $N(R_{35})_2$, $NR_{35}CONR_{37}$, $NR_{35}CON(R_{37})_2$, $NR_{35}SO_2R_{38}$, $NR_{35}SO_2N(R_{37})_2$, $(CH_2)_{0-4}CO_2R_{35}$, $(CH_2)_{0-4}CON(R_{35})_2$, $(CH_2)_{0-4}SO_2N(R_{35})_2$, $(CH_2)_{0-4}SO_2R_{38}$, and C_{1-4} alkyl;

D) R_{35} and R_{37} are each independently selected from hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, $(CH_2)_{0-4}CF_3$; and

E) R_{38} is selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, and $(CH_2)_{0-4}CF_3$;

h) X is oxygen or sulfur; and

i) Q is oxygen or nitrogen; provided that when Q is oxygen R_{13} does not exist.

9. (**Withdrawn**) A method for selecting calcium T-channel antagonists having a desired pharmacological profile, comprising:

testing candidate compounds to measure rapidity of onset of activity;

testing candidate compounds to measure duration of activity; and

selecting candidate compounds having a slower onset of activity and a longer duration of activity than Mibefradil.

10. (**Withdrawn**) The method of Claim 9, wherein at least one of the testing steps is performed *in vitro.*

11. (**Withdrawn**) The method of Claim 9, wherein at least one of the testing steps is performed *in vivo.*